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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/674,975	11/07/2000	David B. Agus	MSKP039	8051

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EXAMINER	
UNGAR, SUSAN NMN	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 01/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/674,975	Applicant(s) Agus et al
	Examiner Ungar	Art Unit 1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Oct 29, 2003* .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *9-13, 16, 17, and 21-24* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *9-13, 16, 17, and 21-24* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *1*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

1. The Amendment filed October 29, 2003 in response to the Office Action of .July 29, 2003 is acknowledged and has been entered. Previously pending claims 1-8, 14-15, 18-20 have been canceled, claims 9, 12, 13 have been amended. Claims 9, 10, 11-in-part as drawn to SEQ ID NO:1, 12, 13, 16-17, 21-24 are currently being examined.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. As drawn to the restriction requirement, Applicant notes that claims 9-10 are generic with respect to the two identified SEQs and it would be appropriate to recombine the other sequence ID which is in essence a separate species from the elected Sequence ID, so as to avoid issuance of two separate patents directed to a genus and a species. The argument has been considered but has not been found persuasive. Applicant correctly pointed out in Paper No. 11 that the original restriction requirement, directed to linked groups according to US practice, was not in accordance with PCT practice. Accordingly, Examiner redrew the restriction requirement with a complete explanation as to why there was a lack of unity. Examiner notes once again that Applicant is incorrect, under PCT practice, the two sequences are not species, one of the other, but rather are separate inventions. Under PCT practice, the two sequences are appropriate separated into different groups and for the reasons set forth previously and above, the restriction requirement is deemed to be proper and is therefore made FINAL.

4. The following objections are maintained:

Objection to the specification, page 1 is maintained because no amendment has been made to reflect the parent provisional application and its status.

Claim Rejections - 35 USC § 112

5. Claims 9, 10, 11-in-part as drawn to SEQ ID NO:1, 12, 13, 16-17, 21-24 remain rejected under 35 USC 112 for the reasons previously set forth in the paper mailed July 29, 2003, Section 8, pages 9-15.

Applicant argues that SEQ ID NO:1 is not the only specific example of a partial sequence that would function as claimed since SEQ ID NO:2 is also a specific example of a partial CD20 sequence, thus the invention as broadly claimed is enabled. The argument has been considered but has not been found persuasive because the specification specifically states that both SEQ ID NO:1 and 2 consist of amino acids 136-179 of the human/murine CD20. Although the sequences of SEQ ID NO:1 and SEQ ID NO:2 are different, it would be expected that the conformational epitope found in SEQ ID NO:2 would be highly similar to that of SEQ ID NO:1, given that the two sequences are species homologues. Therefore, the specification enables, for the reasons of record, only the single comformational epitope of the peptide consisting of SEQ ID NO:1 or the full length CD20 molecule.

Applicant argues that while Examiner has noted the CD20 partial sequences in Table 1, she has not offered any reasons why these do not provide additional scope of enablement. The argument has been considered but has not been found persuasive because contrary to Applicant's argument Examiner has offered both objective evidence and sound scientific reasoning as to why the partial sequences of

Table 1 do not provide additional scope of enablement. It is suggested that Applicant refer to the prior action, pages 13-14.

Applicant argues that Examiner has not looked at the entire invention and that an inventor should be allowed to dominate the future patentable inventions of others where those inventions were based in some way on his teachings. Applicant further argues that under the Examiner's application of 112, Applicant would be obligated to mention and test every conceivable sequence in order to obtain full coverage for their invention. The argument has been considered but has not been found persuasive for the reasons set forth previously and above, Applicant has not enabled the broadly claimed invention. Further, Applicant has not provided guidance as to how to make other fragments that would function as claimed, especially in view of the teachings of Roitt et al, of record, Holmes et al, of record, Herbert et al, of record, Hooijberg et al of record. Applicant suggests that Examiner would require testing of every conceivable sequence in order to obtain full coverage for their invention. This is random experimentation. However, the specification does not provide guidance on how to make the claimed invention and Applicant is correct, in the absence of this teaching, random experimentation is required. Random experimentation is undue.

Applicant argues that other CD-20 specific sequences are known. Hooijberg actually demonstrates the importance of the present invention in breaking tolerance since it shows that mouse epitopes alone do not generate a T-cell response to CD20 in mice. However, the mouse sequences tested in the present invention, which span several of the ineffective sequences of Hooijberg was shown to be effective, thus

the invention has utility. The argument has been considered but has not been found persuasive, the claims as written read on the Hooijberg sequences. The fact that they were found to be ineffective supports Examiner's position. It appears that the findings in the application are unexpected and therefore, the broadly claimed invention is not enabled.

The arguments have been considered but have not been found persuasive and the rejection is maintained.

Claim Rejections - 35 USC § 103

6. Claims 9, 10, 11-in-part as drawn to SEQ ID NO:1, 12, 13, 16-17, 21-24 remain rejected under 35 USC 103 for the reasons previously set forth in the paper mailed July 29, 2003, Section 10, pages 16-19.

Applicant argues that obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention absent some teaching, suggestion of incentive supporting the combination, and recites case law. The argument has been considered but has not been found persuasive because the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference and it is not that the claimed invention must be expressly suggested in any one or all of the references; but rather the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). Applicant's claimed invention fails to patentably distinguish over the state of the art represented by the cited references taken in combination for the reasons of record.

Applicant argues that Examiner has used hindsight knowledge of Applicants invention and does not present a *prima facie* case of obviousness. None of the references Maloney, Kwak, '731 patent is specific for the claimed invention. Further, if persons skilled in the art thought that simply using CD20 with a carrier protein and an adjuvant as now claimed, would have been successful, they would have done so, rather than exploring the much more difficult and costly avenues reflected in Maloney and Kwak. The argument has been considered but has not been found persuasive because it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. In re McLaughlin , 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). However, clearly, it was well known in the art that CD20 is an excellent target for antibody-directed therapies for B-cell lymphoma, non Hodgkin's lymphoma as taught by Maloney et al. Further, Maloney et al teach successful passive immunization treatment of non-Hodgkin's lymphoma while pointing to the need for a CD20 therapy that is not patient-specific. Further, it was well known in the art that B-cell lymphoma, non-Hodgkin's lymphoma is successfully treated by active immunization by B-cell lymphoma antigen conjugated to KLH as taught by Kwak et al. In addition, Kwak, like Maloney specifically points to limitations of autologous vaccine. Finally, it was well known in that art that polypeptide comprising SEQ ID NO:1 is useful for immunotherapeutic applications including

the treatment of plasma neoplasms and treatment of immune mediated diseases which clearly reads on B-cell lymphoma, wherein the CD20 antigen is specifically cited for said immunotherapeutic application. Given the explicit suggestion in both Maloney and Kwak that techniques be established in order to provide general applicability for immunotherapy for B-cell lymphoma, given the teaching of the '731 wherein CD20 is specifically disclosed as an antigen useful for active immunotherapy of plasma neoplasms and immune-mediated diseases, it would have been *prima facie* obvious to combine the references for the reasons of record. Although Applicant asks why the invention was not made previously, this question is not relevant to the issue at hand, given the clear teachings of the prior art references. The arguments have been considered but have not been found persuasive and the rejection is maintained.

7. All other objections and rejections recited in the paper mailed July 29, 2003 are withdrawn.

8. No claims allowed.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT

TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (703) 305-2181. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, PhD, can be reached at (703) 308-6564. The fax phone number for this Art Unit is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1642.

Susan Ungar
Primary Patent Examiner
January 15, 2004